Health Literacy and Anticoagulation-related Outcomes Among Patients Taking Warfarin

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BACKGROUND: Little is known about whether health literacy affects anticoagulation-related outcomes.

OBJECTIVE: To assess how health literacy is associated with warfarin knowledge, adherence, and warfarin control (measured by the international normalized ratio [INR]).

DESIGN: Survey.

PARTICIPANTS: Patients taking warfarin through an anticoagulation clinic.

MEASUREMENTS: Health literacy was measured using the short-form Test of Functional Health Literacy in Adults (s-TOFHLA), dichotomized as "limited" (score 0 to 22) and "adequate" (score 23 to 36). We asked patients to answer questions relating to their warfarin therapy and used multivariable logistic regression to assess whether health literacy was associated with incorrect answers. We also assessed whether health literacy was associated with nonadherence to warfarin as well as time in therapeutic INR range.

RESULTS: Bilingual research assistants administered the survey and s-TOFHLA to 179 anticoagulated English- or Spanish-speaking patients. Limited health literacy was associated with incorrect answers to questions on warfarin's mechanism (adjusted odds ratio [OR] 4.8 [1.3 to 17.6]), side-effects (OR 6.4 [2.3 to 18.0]), medication interactions (OR 2.5 [1.1 to 5.5]), and frequency of monitoring (OR 2.7 [1.1 to 6.7]), after adjusting for age, sex, race/ethnicity, education, cognitive impairment, and years on warfarin. However, limited health literacy was not significantly associated with missing warfarin doses in 3 months (OR 0.9 [0.4 to 2.0]) nor with the proportion of person-time in therapeutic INR range (OR 1.0 [0.7 to 1.4]).

CONCLUSIONS: Limited health literacy is associated with deficits in warfarin-related knowledge but not with self-reported adherence to warfarin or INR control. Efforts should concentrate on investigating alternative means of educating patients on the management and potential risks of anticoagulation.

KEY WORDS: health literacy; anticoagulation; knowledge; adherence.
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Health literacy is the degree to which individuals can obtain, process, and understand the information and services necessary to make appropriate decisions involving their health.[1] Limited health literacy is prevalent in certain populations in the United States, such as the elderly,[2,3] and is associated with receiving fewer preventive services, difficulty following medication instructions, and in some studies, with poorer health outcomes.[4–10] Health literacy may be of particular importance under conditions that involve substantial patient-provider discussion of risks and benefits and in those requiring complex management. One such therapy is anticoagulation with warfarin.

Warfarin therapy requires frequent monitoring and dose changes to maintain anticoagulation intensity within a narrow therapeutic window; anticoagulation outside of the therapeutic range can compromise treatment efficacy if too low and increase hemorrhage risk if too high.[11] It is crucial to educate patients about the risks and benefits of anticoagulation and ensure that they understand how to take warfarin, understand that warfarin can interact with other medications, and understand the importance of regular monitoring. Yet, even in the setting of dedicated anticoagulation clinics, warfarin control is frequently suboptimal.[12,13] Some studies have indicated that poorer patient knowledge about warfarin and lack of education from providers are associated with worse anticoagulation control and increased frequency of hemorrhagic events.[14,15] Lack of knowledge about the indication for warfarin has also been associated with nonadherence with warfarin therapy.[16] Nonadherence to warfarin has been linked to more variable anticoagulation control.[17,18] There is also evidence that even if patients are compliant with therapy, the dose and schedule of what they actually take can differ from the prescribed regimen; this "discordant care" may result from lapses in patient-physician communication.[19]

Few studies have examined the prevalence of limited health literacy among anticoagulated patients or examined whether health literacy is associated with anticoagulation knowledge and control of warfarin therapy. This is of importance because patient educational brochures about anticoagulants are frequently written at a ninth-grade educational level or higher.[20] Clinicians should be certain that patients understand the risks and benefits of a therapy before the treatment commences. For a potentially dangerous medication such as warfarin, it is imperative that patients' understanding and participation in clinical decision making are maximized. Identifying factors associated with poor understanding of treatment decisions and nonadherence to therapies could potentially guide educational initiatives to help inform patients about their care. A study of 143 patients taking warfarin demonstrated that patients with lower numeracy skills had higher variability of their anticoagulation control.[21] However, this study was restricted to patients who spoke English and failed to adjust for potential confounders such as race/ethnicity, sex, and duration of anticoagulation.

To address these concerns, we conducted a study among an ethnically diverse group of patients followed in an anticoagulation clinic to assess whether health literacy is associated with patients' basic knowledge about warfarin, including mechanism and side-effects, as well as self-reported adherence to therapy and anticoagulation control.

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METHODS

We surveyed consecutive eligible patients receiving care in a cardiologist-supervised, pharmacist-staffed anticoagulation clinic at San Francisco General Hospital between March 2002 and June 2003. This clinic serves an ethnically diverse and generally low-income patient population and manages approximately 400 patients at any given time. For non-English speakers, professional interpreter services are generally available. Individual patients who have agreed to take warfarin are referred to the anticoagulation clinic by a primary physician or cardiologist. Once enrolled in the clinic, each patient meets with a staff pharmacist and receives individualized verbal education from a pharmacist regarding the risks and side effects of warfarin therapy as well as a 1-page multilingual patient information sheet developed by Dupont pharmaceuticals. The brochure requires approximately an eighth-grade reading level, assessed by the SMOG grade formula.[22] Anticoagulation clinic staff use a standardized treatment algorithm to adjust warfarin doses based on measurements of the international normalized ratio (INR). International normalized ratio checks are performed approximately every 4 to 6 weeks with phlebotomy performed at the time of the visit; dosing changes and follow-up visit appointments are set up at the time of the visit. At each patient encounter, clinic pharmacists document the patient's updated regimen.

Surveys were verbally administered by bilingual research assistants who spoke English, Spanish, or Cantonese. Informed consent was obtained from patients before enrollment, and patients were offered US$5 for their participation. Patients were eligible if they were aged 18 years or older, spoke English, Spanish, or Cantonese fluently, and had been taking warfarin continuously for at least 3 months. The indication and target range of anticoagulation were obtained from the anticoagulation clinic database. Other data, including on race/ethnicity and education, were obtained via self-report. We excluded patients with ICD-9 diagnoses of psychotic disorder, dementia, blindness, severe aphasia, or were too ill to participate, or had a corrected visual acuity of 20 of 100 or worse. Because health literacy and recall may be affected by undiagnosed cognitive deficits, we measured cognitive ability using the shortened form of the Cognitive Abilities Screening Instrument (s-CASI), which has been validated in international dementia studies, does not require literacy, and has been shown to accurately measure cognition cross-culturally.[23] We defined cognitive impairment as a score of <17.

Measurement of Health Literacy

Functional health literacy was measured at the time of interview using the abbreviated form of the Test of Functional Health Literacy in Adults (s-TOFHLA),[24] a 36-item timed reading comprehension test available in English and Spanish. We administered the s-TOFHLA to English or Spanish speakers, as the test has been validated only in these 2 languages. People scoring between 0 and 16 often misread simple materials such as prescription bottles or appointment slips. Scores of 17 to 22 correspond to problems with more difficult materials such as educational brochures or informed consent documents. Because warfarin therapy requires more complex patient understanding, we considered s-TOFHLA scores of 22 and less as *limited* health literacy and scores of 23 and higher as *adequate* health literacy.[25]

Warfarin Knowledge and Self-reported Adherence

We adapted from prior studies 4 questions that addressed specific features of anticoagulation important for the safe use of warfarin.[26,27] Because atrial fibrillation is a common indication for warfarin therapy, we also asked patients with atrial fibrillation whether their physicians had told them they had atrial fibrillation, whether they knew atrial fibrillation increased their risk for stroke, and whether they knew it was an abnormal heart rhythm. Questions were in multiple-choice format written in layperson terms with a single correct answer. To ensure the quality of translations, all questions were translated into Chinese and Spanish and back-translated into English until concordance in meaning was obtained.

Because anticoagulation therapy requires understanding risks and benefits, requires frequent medication dosing changes, and is monitored using a numerical value (the INR), the ability to understand basic probability, and numerical concepts ("numeracy") can reasonably be considered a component of appropriate anticoagulation knowledge. Therefore, we also developed 4 warfarin-specific numeracy-related questions.

Adherence to warfarin therapy was assessed using a validated questionnaire that asked patients to report the last time they missed taking a warfarin pill, as well as whether they missed a dose within the last 2 weeks and within the last 3 days.[28,29]

Assessment of INR Control

We assessed INR control by calculating the time in therapeutic range for each patient using an adapted linear interpolation method, defined as the proportion of person-time within the target therapeutic range over the total person-time of follow-up.[30] We excluded INRs obtained during interim hospitalizations. Because patients with inconsistent follow-up may systematically differ from those with more regular follow-up, we also performed a subgroup analysis on those patients with an INR measurement at least every other month.

Statistical Analysis

Bivariate comparisons between patients with adequate and limited health literacy were performed using t-tests for continuous variables and χ^2 tests for categorical variables. We used simple logistic regression to determine the association between limited health literacy and incorrect answers to questions related to warfarin therapy, as well as the association with self-reported adherence. Subsequently, we used multivariable logistic regression to control for potential confounders, including age, sex, race/ethnicity, education, number of years on warfarin, and cognitive impairment (by s-CASI score). Race/ethnicity and education were both analyzed as categorical variables. Because primary spoken language was highly collinear with race/ethnicity, we did not include language in the final model. To determine whether health literacy was associated with time in therapeutic INR range, we used Generalized Linear Models to obtain unadjusted and adjusted associations.[31]

This study was approved by the Human Subjects Committee of the University of California, San Francisco.

RESULTS

We approached 300 potentially eligible patients in the anticoagulation clinic for participation in the study. Of these, 30 were excluded because they were too ill to participate, had their medications filled elsewhere, were on nonformulary warfarin, or had poor visual acuity. Forty-nine declined participation or failed to complete the interview. We also did not include in this study 42 patients whose primary language was other than English or Spanish, as we were not able to administer the s-TOFHLA to these patients.

The characteristics of the final 179 interviewed patients are shown in Table 1. Patients were of diverse race/ethnicities (34.1% Latino, 24.6% Asian American/Pacific Islander, 16.8% African American), and 33.5% reported having no more than an eighth-grade-level education. The most common indications for anticoagulation were atrial fibrillation or mechanical valve (72.3% of patients). The prevalence of limited health literacy was 60.9%, and the median s-TOFHLA score was 17 (interquartile range 5 to 31). When compared with subjects with adequate health literacy, patients with limited health literacy were more likely to be older, female, nonwhite, have less than a high-school education, be taking warfarin for a longer period of time, and score less than 17 on the s-CASI (Table 1).

Table 1. Characteristics Of 179 Patients Taking Warfarin, Comparing Patients With Limited Health Literacy (s-TOFHLA 0 to 22) to Adequate Health Literacy (s-TOFHLA 23 to 36)

	Limited Health Literacy $n=109$ Mean (95%CI) or *N* (%)	Adequate Health Literacy $n=70$ Mean (95%CI) or *N* (%)	*P* Value
Age, years	63.3 [61.0 to 65.6]	53.8 [50.4 to 57.1]	<.001
Female	57 (52.3)	27 (38.6)	.07
Race			<.001
Latino	50 (45.9)	11 (15.7)	
Asian-Pacific Islander	31 (28.4)	13 (18.6)	
White	11 (10.1)	25 (35.7)	
African American	14 (12.8)	16 (22.9)	
Other	3 (2.8)	5 (7.1)	
Most comfortable language			<.001
English	22 (20.2)	43 (61.4)	
Spanish	50 (45.9)	12 (17.1)	
Tagalog	21 (19.3)	11 (15.7)	
Other	16 (14.7)	4 (5.72)	
Education			<.001
≤8th grade	55 (50.5)	5 (7.1)	
Some or all of high school	33 (30.3)	21 (30.0)	
≥College	21 (19.3)	44 (62.9)	
s-CASI <17	31 (19.3)	2 (1.4)	<.001
Years on warfarin	4.4 [3.4 to 5.3]	2.9 [2.0 to 3.8]	.04
Indication for warfarin*			.17
Atrial fibrillation	56 (51.4)	27 (39.7)	
Mechanical valve	28 (25.7)	17 (25.0)	
Thromboembolism or hypercoagulable state	25 (22.9)	24 (35.3)	

*Indications unknown for 2 subjects.
s-CASI: short form Cognitive Abilities Screening Instrument; CI, confidence interval; OR, odds ratio.

Warfarin Knowledge

Patients with limited health literacy were more likely to have incorrect answers to most questions addressing warfarin-related knowledge and numeracy (Table 2). After multivariable analysis, limited health literacy was significantly associated with incorrect answers for all of the knowledge and most of the numeracy questions, even after adjusting for age, sex, race/ethnicity, education, cognitive impairment, and number of years on warfarin (Table 2). Of patients who were taking warfarin for atrial fibrillation, those with limited health literacy were more likely to report that their doctor had not told them they had atrial fibrillation (60% vs 9.7%, $P<.001$), less likely to know that their condition increased their risk for stroke (42% vs 70%, $P=.008$), and less likely to know that atrial fibrillation is an abnormal heart rhythm (56% vs 82%, $P=.06$).

Adherence to Warfarin Therapy and INR Control

Limited health literacy was not significantly associated with self-reported adherence in either unadjusted or adjusted analyses (Table 3). In general, self-reported adherence to therapy was reasonably high, with 57.0% of patients reporting that they had not missed a dose in more than 3 months.

In the analysis of INR control, we excluded 1 patient who did not have more than 3 months of INR data available for analysis. The mean number of INRs drawn over the previous 12-month period was 11.5 ($\pm$ SD 5.2) and most patients (66.3%) had INR measurements at least every other month. There were no significant differences between patients with INR measurements at least every other month and patients with less regular follow-up in terms of health literacy, age, sex, or s-CASI score. Those with less regular follow-up were more likely to be Latino than white (48% vs 28%, $P=.001$).

Patients with limited health literacy did not differ significantly from those with adequate health literacy in terms of the time within the therapeutic INR range over the previous 12 months (Table 3). Restricting the analyses to the subgroup of patients with INRs drawn at least every other month did not significantly change our results.

DISCUSSION

Patients in this anticoagulation clinic who had limited health literacy were more likely than those with adequate health literacy to give incorrect answers on general questions relating to their warfarin therapy. However, limited health literacy was not significantly associated with either self-reported adherence to warfarin or INR control.

It warrants concern that a substantial proportion of subjects followed for chronic warfarin therapy could not answer basic questions about warfarin, especially given the potentially high-risk nature of anticoagulation treatment. Limited health literacy may be a marker for factors that are associated with whether a patient receives or understands warfarin teaching, such as the quality of oral communication, especially in the domains of explanatory and participatory communication.[32–34] Alternative means of communicating the risks and benefits of high-risk therapies such as warfarin should be investigated. Safe management of warfarin includes ensuring that patients know what specific factors can affect their warfarin control, such as changes in medication regimen or diet. The current study highlights the need for clinicians to assess patients' understanding of how and why to take medications, both to optimize appropriate dosing and anticoagulation management as well as to ensure that patients are informed about the

Table 2. Likelihood Of An Incorrect Answer To Questions Regarding Warfarin, Comparing Patients With Limited Health Literacy to Those With Adequate Health Literacy

	% Patients With Incorrect Answer		Likelihood of Incorrect Answer	
	Limited Health Literacy	Adequate Health Literacy	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)
Warfarin-related knowledge questions				
How does warfarin work? *Answer: thins the blood	30.3	5.7	7.2 [2.4 to 21.3]	4.8 [1.3 to 17.6]
What is the most common problem of taking warfarin? *Answer: bleeding or bruising easily	51.4	14.3	6.4 [2.9 to 13.7]	6.4 [2.3 to 18.0]
Which of the following is true about how warfarin works? *Answer: some medications interfere with how warfarin works	65.1	35.7	3.4 [1.8 to 6.3]	2.5 [1.1 to 5.5]
If your blood test results for warfarin are "good," how often you should see the doctor here in the anticoagulation clinic? *Answer: about once every 1 to 2 mo	34.9	27.1	1.4 [0.7 to 2.8]	2.7 [1.1 to 6.7]
Warfarin-related numeracy questions				
If your blood test result for warfarin is just right when it is between 2.0 and 3.0, which of the following results would be "just right?"	70.6	25.7	7.0 [3.5 to 13.7]	2.6 [1.1 to 6.1]
Let's say you take 1 tablet of warfarin every night from Monday to Saturday and 2 tablets on Sundays, and let's say your next appointment here is 1 wk from today. Exactly how many pills would you take from today until your next appointment?	73.4	35.7	5.0 [2.6 to 9.5]	1.9 [0.8 to 4.4]
Let's say your dose is 1 6 mg tablet a day from Monday to Saturday, and 2 6 mg tablets on Sundays. How many milligrams would you take on Sundays?	50.5	18.6	4.5 [2.2 to 9.1]	3.2 [1.3 to 7.7]
Let's say your doctor tells you that you have a 10% risk of stroke, and that taking warfarin would lower your risk of stroke by one-half. If you agree to take warfarin, what would be your new risk of stroke?	71.6	18.6	11.0 [5.3 to 22.9]	5.7 [2.3 to 14.0]

Note: Questions were in multiple-choice format with a single correct answer.
**Adjusted for age, sex, race/ethnicity, education, years on warfarin, and s-CASI score.*
s-CASI: short form Cognitive Abilities Screening Instrument.

therapy's risks and benefits. Limited health literacy is frequently underappreciated in general practice,[35] with assumptions that patients are able to comprehend written educational materials and oral clinical communication about their medical conditions and treatment plans. Whether alternative forms of patient education, such as video-assisted instruction, improvements in verbal communication, or visual instruction techniques, can help improve patient understanding needs to be investigated.

While limited health literacy was associated with knowledge deficits in our study, literacy did not appear to be associated with self-reported adherence or warfarin control. It is possible that anticoagulation clinics can standardize anticoagulation treatment enough to reduce potential disparities that may arise from differences in patients' understanding of the specifics of warfarin management. This may be similar to diabetes care, where implementation of a comprehensive disease management program appeared to have greater benefit in patients with lower literacy.[36]

Owing to the increasing complexity of medical care involving the management of multiple medications and complicated disease-modification counseling, clinicians report having little time during office visits to devote to patient education. Our study suggests that additional barriers to shared decision making may occur when patients have limited health literacy. It is also possible that barriers to communication and comprehension contribute to the undertreatment or withholding of therapy among eligible patients, a phenomenon that disproportionately affects the elderly and racial/ethnic minorities.[26,27] Our study sampled patients who were deemed able and willing to take long-term anticoagulation; patients who declined therapy or discontinued warfarin were not represented. It is conceivable that patients with the least understanding of the risks and benefits of anticoagulation were less likely to be offered the option of warfarin therapy in the first place.

There are several limitations to this study. First, because this was an observational study, we could not determine whether there was a causal association between limited health

Table 3. Self-Reported Adherence And INR Control, Comparing Patients With Limited To Adequate Health Literacy

	Limited Health Literacy (%)	Adequate Health Literacy (%)	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)
Self-reported adherence				
Missed a dose within the last 3 d	6.5	17.1	0.6 [0.2 to 1.7]	0.5 [0.1 to 2.1]
Missed a dose within the last 2 wk	12.0	14.3	0.6 [0.3 to 1.4]	0.7 [0.3 to 2.2]
Did not miss a dose in > 3 mo	61.1	51.4	1.5 [0.8 to 2.7]	0.9 [0.4 to 2.0]
Person-time in therapeutic INR range	45.0	43.2	1.2 [0.9 to 1.5]	1.0 [0.7 to 1.4]

**Adjusted for age, sex, race/ethnicity, education, years on warfarin, and s-CASI score.*
INR: international normalized ratio; s-CASI: short form Cognitive Abilities Screening Instrument.

literacy and lack of anticoagulation knowledge. Additionally, we had no direct measures of clinician-patient communication and/or the quality of shared decision making experienced by the subjects. Second, while we only enrolled subjects who reported being fluent in English or Spanish, we did not directly measure spoken English fluency, which may affect the interpretation of results of health literacy and anticoagulation knowledge scores among the nonnative English speakers. Third, although our measures of knowledge were based on issues highly relevant to warfarin therapy and adapted from prior warfarin studies,[28,29] more in-depth qualitative interviews may provide greater insights into the degree of knowledge deficit or belief systems. Fourth, our measure of adherence was by self report, which may be subject to recall bias, social desirability, and mismeasurement. In fact, our own research demonstrates that patients with limited health literacy are more likely than those with adequate health literacy to report adhering to a warfarin regimen that is inconsistent with that of the prescribing clinician, calling into question the reliability and validity of self-reported adherence measures in this population.[37] Due to the small sample size, we were not able to assess for thromboembolic or hemorrhagic complications associated with anticoagulation knowledge and/or health literacy. However, because previous studies show that anticoagulation control is strongly correlated with hemorrhagic complications on warfarin, we felt that INR was a reasonable proxy for hemorrhagic risk.[38,39] Finally, although this was an ethnically diverse group of patients, the study took place in a single medical center serving a largely indigent population and may not be generalizable to other populations.

In conclusion, a significant proportion of patients followed in an ethnically diverse anticoagulation clinic had deficits in knowledge relating to their anticoagulation therapy. Limited health literacy was strongly associated with knowledge deficits, although it was not significantly associated with either self-reported adherence to warfarin or overall anticoagulation control. Further studies should investigate alternative means of communicating the risks and benefits of anticoagulation management to help improve patient understanding, informed decision making, and the safe use of warfarin.

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